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Research Article

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Knowledge, Attitudes, and Practices of Pharmacists toward Vitamin B12 Deficiency Associated with Metformin Use: A Cross-Sectional Survey Study

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ABSTRACT

Metformin, a first-line therapy for type 2 diabetes mellitus (T2DM), is linked to vitamin B12 deficiency with long-term use (≥1,500 mg/day), increasing risks of neuropathy and megaloblastic anaemia. Community pharmacists, as accessible healthcare providers, are well-positioned to promote screening and education to mitigate these risks.

This cross-sectional survey was conducted among 100 pharmacists in Tripoli, Libya, using a structured self-administered questionnaire to assess their knowledge, attitudes, and practices, (KAP) regarding metformin-associated vitamin B12 deficiency. Descriptive statistics summarized responses, with chi-square tests and Pearson's correlation used to examine associations ($P < 0.05$ was considered significant). Participants were predominantly young (mean age 28 ± 6.05 years) with a mean experience of 4.5 ± 5.2 years. Most (87%) recognized metformin's link to B12 deficiency, and 77% identified reduced intestinal absorption. Monitoring was frequent (57% always, 34% sometimes recommended screening; 65% observed deficiency cases). Awareness was significantly associated with counselling frequency ($\chi^2 = 7.76$, $P = 0.041$) and case observation ($\chi^2 = 8.27$, $P = 0.004$), while Practices were correlated with accurate symptom identification ($\chi^2 = 16.43$, $P < 0.001$) and improved patient adherence to monitoring ($\chi^2 = 8.22$, $P = 0.037$). Positive attitudes (86% felt responsible for education) linked to better adherence outcomes ($\chi^2 = 12.70$, $P < 0.001$). Experience positively correlated with KAP ($r > 0.22$, $P < 0.05$). Barriers included patient disinterest (29%) and time constraints (19%). While pharmacists demonstrated strong awareness and engagement, structured training programs and national guidelines are needed to optimize counselling and improve patient outcomes.

***Key words**: Metformin; Vitamin B12 deficiency; Pharmacists; Type 2 diabetes mellitus; Patient counselling.*

INTRODUCTION

Libya faces a substantial diabetes burden, with 15.8% adult prevalence in 2024, ranking among the highest in North Africa and approximately one-third of cases undiagnosed.[1] This high prevalence, coupled with limited healthcare infrastructure, places significant strain on the nation's resource-constrained system. Type 2 diabetes mellitus (T2DM), the predominant form, requires effective management to prevent complications such as cardiovascular disease, neuropathy, and nephropathy. Metformin (dimethyl biguanide), the cornerstone first-line therapy for T2DM, reduces blood glucose by enhancing insulin sensitivity, suppressing hepatic glucose production, and promoting modest weight loss, making it widely prescribed in Libya and globally.[2,3]However, prolonged metformin use (≥1,500 mg/day, ≥3 years) is associated with an increased risk of vitamin B12 deficiency, primarily due to impaired receptor-mediated absorption in the ileum's intrinsic factor-cobalamin complex.[3-5] This risk is further exacerbated by concomitant use of proton pump inhibitors, common in T2DM patients for managing comorbidities like gastroesophageal reflux.[6,7]

Vitamin B12, a water-soluble micronutrient, is critical for DNA synthesis, red blood cell formation, and neurological function, with absorption occurring via passive diffusion (1–2% of oral dose) and active receptor-mediated processes in the small intestine.[8,9] Deficiency manifests as megaloblastic anaemia (characterized by fatigue, pallor, and shortness of breath), neurological symptoms (peripheral numbness, memory impairment, and cognitive decline), and gastrointestinal disturbances (glossitis, anorexia), which can overlap with or exacerbate T2DM complications.[10,11] If untreated, B12 deficiency may lead to irreversible neuropathy, cognitive deficits, and increased healthcare costs, posing a significant public health challenge.[12] The American Diabetes Association

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recommends routine B12 monitoring for T2DM patients on long-term metformin, particularly older adults or those with neuropathy or unexplained anaemia, to mitigate these risks.[2] Community and hospital pharmacists, as highly accessible healthcare providers, are uniquely positioned to bridge this gap. Their frequent patient interactions enable them to identify at-risk individuals, promote B12 screening, educate patients on deficiency symptoms, and recommend supplementation when appropriate.[13] In the Libyan healthcare system, where physicians face heavy workloads and the pharmacy workforce is predominantly young and community-based.[14] pharmacists play an increasingly important role in chronic disease management. However, both locally and globally, their involvement in routine monitoring and management of metformin-associated vitamin B12 deficiency remains insufficiently investigated.[15,16] Although numerous studies have explored the prevalence, mechanisms, and clinical impact of metformin-induced vitamin B12 deficiency from the patient perspective,[17–20] limited research has examined pharmacists' knowledge, attitudes, and practices regarding this issue.[21] This gap restricts the design of effective pharmacist-led strategies to enhance patient outcomes.

This cross-sectional study of pharmacists in Tripoli, Libya, aims to evaluate their awareness of metformin-associated vitamin B12 deficiency, assess their practices in recommending B12 monitoring and supplementation, and explore their attitudes toward their role in patient education and chronic disease management. By identifying barriers to effective management, such as patient disinterest or time constraints, this study seeks to inform targeted educational strategies and interprofessional collaborations to enhance pharmacists' contributions to T2DM care in Libya's resource-constrained healthcare system.

MATERIALS AND METHODS

This cross-sectional observational study was conducted in Tripoli, Libya, from April to June 2025, to assess pharmacists' awareness, practices, and attitudes toward metformin-associated vitamin B12 deficiency. Data were collected using a structured, validated 19-item questionnaire developed based on published literature and international clinical guidelines.[22,24] A convenience sample of 100 licensed pharmacists was engaged from community and hospital pharmacies in both public and private sectors across Tripoli. Eligibility criteria included holding an active pharmacy license and current employment in community, hospital, or clinical practice settings. Non-practicing pharmacists and those working outside Tripoli were excluded to ensure population consistency.

The questionnaire, developed through literature review and expert consultation, comprised four sections: (1) demographics (age, gender, years of experience, practice setting, pharmacy location); (2) awareness (knowledge of metformin-B12 deficiency link, mechanisms, symptoms, information sources); (3) practices (frequency of recommending B12 monitoring, experience with deficiency cases, counselling actions, estimated weekly metformin patients, perceived barriers); and (4) attitudes (perceived responsibility for monitoring, importance of patient education, preferred professional information sources). The self-administered questionnaire was distributed in person, with trained undergraduate pharmacy students available to clarify any questions to ensure comprehension and accuracy. Participation was voluntary, anonymous, and without incentives. Consent was obtained prior to participation, and confidentiality was maintained in accordance with the ethical standards.

Data were analysed using the Statistical Package for the Social Sciences (SPSS) version [version 29.1.1; (IBM Corp., Armonk, NY, USA).]. Descriptive statistics, including frequencies, percentages, means, and standard deviations, were used to summarize participant characteristics and responses. Associations between categorical variables (e.g., awareness, practice, and attitude) were evaluated using the chi-square (χ^2) test, while Pearson's correlation coefficient (r) assessed relationships between continuous variables, including age, years of experience, awareness, practice, and attitude scores. Statistical significance was set at $P < 0.05$. Normally distributed continuous data were presented as mean ± SD, and non-normally distributed data as median and interquartile range (IQR).

RESULTS

Participant Characteristics

Of 100 licensed pharmacists surveyed in Tripoli, Libya, 51% were male (n=51) and 49% were female (n=49), with a mean age of 28.0 ± 6.1 years (range: 22–57 years). Years of experience ranged from <1 to 31 years (mean: 4.5 ± 5.2 years). Participants worked in community (73% private, n=73; 12% public, n=12), hospital (3%, n=3), or combined community-hospital settings (12%, n=12), primarily in Souq Al-Jumaa (34%, n=34), Al-Nofleen (14%, n=14), Hai Al-Andalus (10%, n=10), and other Tripoli districts. Weekly exposure to metformin-treated patients varied: 36% (n=36) managed >50 patients, 29% (n=29) 10–30 patients, 15% (n=15) 31–50 patients and 20% (n=20) <10 patients (Table 1).

Table 1: Demographic Characteristics of 100 Surveyed Pharmacists.

Characteristic	n (%)	Range	Mean ± SD	Median (IQR)
Age (years)	—	22–57	28.0 ± 6.05	27.0 (24.0–31.0)
Years of experience	—	0.003–31*	4.5 ± 5.2	2.0 (1.0–5.0)
Sex				
Male	51 (51%)	—	—	
Female	49 (49%)	—	—	
Work district				
Souq Al-Jumaa	34 (34%)	—	—	
Al-Nofleen	14 (14%)	—	—	
Hai Al-Andalus	10 (10%)	—	—	
Other districts	42 (42%)	—	—	
Employment setting				
Private pharmacy	73 (73%)	—	—	
Public pharmacy	12 (12%)	—	—	
Hospital	3 (3%)	—	—	
Dual roles	12 (12%)	—	—	
Weekly patients prescribed metformin				
< 10	20 (20%)	—	—	
10–30	29 (29%)	—	—	
31–50	15 (15%)	—	—	
> 50	36 (36%)	—	—	

(Note: Minimum experience was recorded as 1 day (≈0.003 years).

Pharmacists' Knowledge (Awareness)

Most pharmacists (87%, n=87) recognized metformin's association with vitamin B12 deficiency; 7% (n=7) were unsure, and 6% (n=6) were unaware. Knowledge sources included scientific references (33%, n=33), academic training (32%, n=32), continuing education (15%, n=15), and clinical guidelines (7%, n=7). Most (77%, n=77) correctly identified reduced small intestine absorption as the deficiency mechanism, while 21% (n=21) selected incorrect mechanisms. For symptoms, 80% (n=80) identified at least one correct symptom, with 54% (n=54) recognizing numbness, 11% (n=11) megaloblastic anaemia, 3% (n=3) memory impairment, and 26% (n=26) multiple symptoms (Table 2).

Table 2: Pharmacists' Knowledge of Metformin-Associated Vitamin B12 Deficiency

Awareness Item	Response Options	n (%)
Awareness of association	No	6 (6%)
	Not sure	7 (7%)
	Yes	8 (7%)
Source of knowledge	Not aware	5 (5%)
	Continuing education	15 (15%)
	Clinical guidelines	7 (7%)
	Scientific references	33 (33%)
	Academic training	32 (32%)
	More than one	8 (8%)
Mechanism	Inhibition in liver	21 (21%)
	Increased renal excretion	2 (2%)
	Decreased absorption (intestine)	77 (77%)
Neurological and Haematological symptoms	I don't know	6 (6%)
	Macrocytic anaemia	11 (11%)
	Numbness in extremities	54 (54%)
	Memory weakness	3 (3%)
	More than one	26 (26%)

Notes: Percentages for "Source of Knowledge" and "Mechanism of Deficiency" sum to 100% within each subcategory. For "Symptom Recognition," respondents could select multiple symptoms, so percentages do not sum to 100%. "Other" sources include unspecified or mixed sources.

Pharmacists' Practices

Pharmacists frequently recommended vitamin B12 monitoring, with 57% (n=57) always and 34% (n=34) sometimes advising patients on metformin to monitor levels; 4% (n=4) rarely and 5% (n=5) never advised monitoring. Most (65%, n=65) reported observing vitamin B12 deficiency cases in metformin users, while 35% (n=35) had not. When suspecting deficiency, 44% (n=44) recommended supplements directly, 42% (n=42) combined supplements with physician referrals, and 14% (n=14) referred to physicians only. No pharmacists reported inaction. Barriers to counselling included lack of patient interest (29%, n=29), time constraints (19%, n=19), limited knowledge (5%, n=5), and perceived lack of responsibility (6%, n=6); 39% (n=39) reported no barriers (Table 3).

Table 3: Pharmacists' Practices toward Metformin-Associated Vitamin B12 Deficiency.

Practice/ Behaviour Item	Response Options	n (%)
Do you advise patients to monitor vitamin B_{12} levels?	I do not advise	5 (5%)
	Rarely	4 (4%)
	Sometimes	34 (34%)
	Always	57 (57%)
Have you noticed/metformin users with B_{12} deficiency?	No	35 (35%)
	Yes	65 (65%)
Action taken when deficiency is suspected	Refer to physician	14 (14%)
	Recommend B_{12} supplements	44 (44%)
	More than one response	42 (42%)
	Do nothing	0 (0%)
Obstacles to counselling	Not my responsibility	6 (6%)
	Lack of knowledge	5 (5%)
	Lack of time	19 (19%)
	Lack of patient interest	29 (29%)
	No obstacles	39 (39%)
	All listed	2 (2%)

Pharmacists' Attitudes

Pharmacists expressed positive attitudes toward their role in addressing vitamin B12 deficiency. Most (86%, n=86) agreed or strongly agreed (44%, n=44; 42%, n=42) that they should inform patients about the risk, with 14% (n=14) neutral. Similarly, 70% (n=70) agreed or strongly agreed (35%, n=35 each) that monitoring B12 levels is their responsibility. Nearly all (93%, n=93) believed that the topic deserves more professional awareness, and 88% (n=88) felt patient education improved adherence. Preferred information sources included social media (40%, n=40), lectures (32%, n=32), articles (12%, n=12), awareness campaigns (5%, n=5), and mixed sources (11%, n=11) (Table 4).

Table 4: Pharmacists' Attitudes toward Metformin-Associated Vitamin B12 Deficiency.

Attitude Item	Response Options	n (%)
Pharmacists should inform patients about risks	Neutral	14 (14%)
	Agree	44 (44%)
	Strongly agree	42 (42%)
Monitoring is the pharmacist's responsibility	Strongly disagree	1 (1%)
	Disagree	3 (3%)
	Neutral	26 (26%)
	Agree	35 (35%)
	Strongly agree	35 (35%)
More pharmacist awareness needed	No	7 (7%)
	Yes	93 (93%)
Educating patients may improve adherence	Disagree	3 (3%)
	Neutral	9 (9%)
	Agree	51 (51%)
	Strongly agree	37 (37%)
Preferred source of information	Social media	40 (40%)
	Medical awareness programs	5 (5%)
	Medical articles	12 (12%)
	Scientific lectures	32 (32%)
	All listed	11 (11%)

Summary of associations Between Knowledge, Practices, Attitudes, and Professional Characteristics

Analysis of associations between knowledge, practice, attitudes, and professional characteristics revealed several significant findings. Pharmacists with higher awareness were more likely to counsel patients on vitamin B_{12} monitoring ($\chi^2 = 7.76$, $P = 0.041$) and greater recognition of deficiency cases among metformin users ($\chi^2 = 8.27$, $P = 0.004$). In terms of professional practice, active counselling was linked to accurate identification of neurological and haematological symptoms of vitamin B_{12} deficiency ($\chi^2 = 16.43$, $P < 0.001$). Additionally, those who actively educated patients about the risk of deficiency were significantly associated with improved patient adherence to metformin therapy ($\chi^2 = 8.22$, $P = 0.037$). Attitudes also played a critical role. Pharmacists who strongly supported the importance of recommending vitamin B12 monitoring were significantly more likely to promote adherence behaviors in their patients ($\chi^2 = 12.70$, $P < 0.001$). Pearson's correlations showed strong positive associations between pharmacists' years of experience and age ($r = 0.861$, $P < 0.001$), and modest but significant correlations were found between years of experience and awareness ($r = 0.272$, $P = 0.006$), as well as attitudes toward patient care ($r = 0.223$, $P = 0.006$). Moreover, awareness was positively correlated with practice ($r = 0.272$, $P = 0.006$), and practice correlated positively with attitudes ($r = 0.282$, $P = 0.004$) (Table 5).

Table 5: Summary of significant associations between Awareness, Practices, Attitudes and experience among pharmacists.

Variables Examined	Significant Associations	Statistical Test	Test Value	p-value
Awareness & B_{12} Monitoring Advice	Higher awareness associated with more frequent patient counselling and follow-up advice	χ^2-test	$\chi^2 = 7.76$	0.041
Awareness & B_{12} Deficiency case recognition	Pharmacists with higher awareness more likely to have observed patients diagnosed with deficiency	χ^2-test	$\chi^2 = 8.27$	0.004
Practices & Symptoms Identifivation	Higher practice associated with correct identification of neurological and hematological symptoms	χ^2-test	$\chi^2 = 16.43$	<0.001
Practices & Patient Education Impact	Patient education significantly associated with improved adherence to metformin therapy	χ^2-test	$\chi^2 = 8.22$	0.037
Attitude & B_{12} Monitoring Recommendation	Positive attitude toward monitoring associated with better adherence	χ^2-test	$\chi^2 = 12.70$	<0.001
Years of Experience & Age	Strong positive correlation	Pearson's r	r = 0.861**	<0.001
Years of Experience & Awareness	Positive correlation	Pearson's r	r = 0.272**	0.006
Years of Experience & Attitudes	Positive correlation	Pearson's r	r = 0.223*	0.006
Awareness & Practices	Positive correlation	Pearson's r	r = 0.272**	0.006
Practices & Attitudes	Positive correlation	Pearson's r	r = 0.282**	0.004

(*$P < 0.05$ = significant; * $P < 0.01$ = *highly significant*.).

DISCUSSION

The study revealed that pharmacists in Tripoli represent a predominantly young and active professional group, with most practicing in private community pharmacies and serving a high volume of patients weekly, indicating significant potential for pharmacist-led interventions in chronic disease management. The predominantly young cohort (mean age: 28.0 ± 6.1 years, mean experience: 4.5 ± 5.2 years) aligns with Libya's pharmacy workforce trends, where younger professionals dominate community settings.[14] Most participants (73%) worked in private community pharmacies, serving high volumes of metformin-treated patients (36% >50 patients/week), consistent with pharmacists' expanding role as primary care providers in diabetes management.[13,25]

The wide experience range (<1–31 years) enabled robust analysis of professional experience's influence on awareness, practices, and attitudes.

Regarding Awareness, pharmacists demonstrated strong awareness, with 87% recognizing metformin's link to vitamin B12 deficiency, a rate higher than in Jordan (72%)[26,27] and Saudi Arabia (68%)[22] but comparable to Tunisia (85%).[17] Most (77%) correctly identified impaired intestinal absorption as the mechanism, aligning with pharmacological evidence.[5,7] However, only 3% recognized cognitive effects, far below global awareness of neurological sequelae[8] and 21% misattributed the cause (e.g., hepatic dysfunction), This gap underscores the need for targeted education on pathophysiology and drug interactions, including proton pump inhibitors (PPIs), which exacerbate B12 malabsorption when co-prescribed with metformin.[7]

Pharmacists exhibited proactive practices, with 91% recommending B12 monitoring (57% always, 34% sometimes). This reflects expanding patient-centred roles in chronic disease care[13,28] as seen in Jordan where pharmacists actively screen and manage medications.[27] Notably, 65% of participated pharmacists reported

observing deficiency cases, indicating suggesting real-world exposure that reinforces proactive behaviour. Barriers included patient disinterest (29%) and time constraints (19%), yet 39% reported no obstacles, a more favourable profile than in the UAE, where lack of physician collaboration was a major barrier.[29]

These findings align with global evidence highlighting pharmacists' expanding role in diabetes management.[3,12,30] Furthermore, pharmacists displayed overwhelmingly positive attitudes toward patient care regarding metformin-associated vitamin B12 deficiency. The vast majority agreed or strongly agreed that they should inform patients about the risk and that B12 monitoring falls within their professional responsibility.[31]

Almost all (93%) believed the issue deserves greater awareness, and 88% recognized that patient education may enhance adherence to metformin therapy. These results align with international studies emphasizing pharmacists' patient-centred perspective and advocacy for shared responsibility in chronic disease management.[32-33]However, the observation that social media served as the predominant information source underscores the need for more structured, evidence-based resources like blended-learning continuing pharmacy education (CPE) programs, which have improved knowledge retention in similar settings[34] and interprofessional workshops, as Toklu and Hussain (2017) argue that traditional pharmacy education is outdated and advocate for problem-based, patient-centred training models to prepare pharmacists for expanded clinical roles.[35]

Statistical analysis confirmed significant inter-relations between knowledge, practice, and attitude dimensions. Higher awareness was significantly associated with more frequent counselling on B12 monitoring ($\chi^2 = 7.76$, $P = 0.041$) and with greater likelihood of observing deficiency cases among metformin users ($\chi^2 = 8.27$, $P = 0.004$).

These associations suggest that knowledge translates directly into more vigilant clinical practice and patient engagement.

Moreover, pharmacists with stronger practice behaviours demonstrated significantly higher recognition of neurological and haematological symptoms ($\chi^2 = 16.42$, $P < 0.001$), and those actively involved in patient education were more likely to report improved adherence outcomes ($\chi^2 = 8.22$, $P = 0.037$). Attitude also played a reinforcing role: pharmacists who expressed stronger responsibility toward monitoring were more likely to counsel patients consistently and to associate their interventions with adherence improvement ($\chi^2 = 12.70$, $P < 0.001$). Correlation analysis demonstrated that years of experience positively correlated with both awareness ($r = 0.272$, $P = 0.006$) and attitudes ($r = 0.223$, $P = 0.006$), awareness and practices ($r = 0.272$, $P = 0.006$), and practices and attitudes ($r = 0.282$, $P = 0.004$), suggesting that practical experience modestly strengthens knowledge and professional outlook. These findings align with prior research indicating that experiential learning enhances pharmacists' confidence and clinical performance.[33,36,37] Overall, the interdependence of awareness, practice, and attitude underscores that improvements in one domain can yield positive ripple effects across others, a critical insight for designing future pharmacist education and intervention programs.[31,34]

Limitations: Its cross-sectional design limits causal inference, and self-reported responses may be influenced by recall or social desirability bias. The Tripoli-based sample and modest size (n = 100) restrict generalizability, and the absence of patient outcome data precludes evaluation of clinical impact. Larger, multi-regional studies are recommended to confirm these findings.

CONCLUSION

Pharmacists in Tripoli demonstrated high awareness, positive attitudes, and proactive practices regarding metformin-induced vitamin B12 deficiency. The majority routinely counselled patients and recognized the clinical implications of long-term metformin use. Significant associations between awareness, practice, and attitude indicate that greater knowledge directly enhances professional behaviour and patient-centred care. Despite these strengths, barriers such as time constraints and limited patient engagement were noted, underscoring the need for structured continuing education programmes, clear national clinical guidelines, and strengthened interprofessional collaboration to optimize pharmacist-led monitoring of vitamin B12 status in metformin users. Given the study's modest sample size and single-city focus, it may serve as a foundation for a larger, multi-centre investigation or pilot intervention study to assess pharmacist-driven interventions and their impact on patient adherence and vitamin B12 status.

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***Conflict of Interest*:**

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